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Patent
Attorney's Docket No. 033172-001

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Patent Application of

WOLPERT et al

Application No.: 09/319,736

Filed: August 2, 1999

For: THERAPEUTIC APPLICATIONS OF ANTIGENS OR EPITOPES ASSOCIATED WITH IMPAIRED CELLULAR PEPTIDE PROCESSING, E.G. EXPRESSED...

Group Art Unit: 1635

Examiner: K. Lacourciere

REPLY & AMENDMENT

Assistant Commissioner for Patents
Washington, D.C. 20231

Sir:

In complete response to the Official Action mailed March 28, 2002, please amend the above-cited application as follows.

IN THE CLAIMS

Please delete claims 83-104 without prejudice or disclaimer.

Please add the following new claims:

143. (New) A method for impairing cellular peptide processing for MHC presentation comprising

treating cells with a substance

wherein the substance is characterized in that tumor cells treated with the substance are subject to specific lysis by CTL elicited by endogenous MHC class I dependent

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antigens of the TAP-deficient variant of said tumor cell which has been transfected with the stimulatory molecule B7-1;

and thereby inducing immunological effector cells specific for endogenous epitopes associated with impaired cellular peptide processing for MHC presentation.

144. (New) The method of claim 143, wherein the substance is selected from the group consisting of substances that inhibit the function of TAP and substances that inhibit the expression of TAP.

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145. (New) The method of claim 143, wherein the substance is selected from the group consisting of ICP47 of HSV type 1, IE 12 of HSV type 2, a gene encoding a TAP inhibitor, a nucleotide sequence that is complementary to mRNA or DNA sequences encoding TAP, antisense oligonucleotides, and RNA destroying ribozyme.

146. (New) The method of claim 143, wherein the substance inhibits the function and/or expression of the proteasome.

147. (New) The method of claim 143, wherein the substance is selected from the group consisting of a peptide aldehyde Z-Leu-Leu-H, Lactacystin, DNA encoding a proteasome inhibitor, a nucleotide sequence that is complementary at least in part to the mRNA or DNA sequences encoding proteasome, antisense oligonucleotides and RNA-destroying ribozyme.

148. (New) A process comprising

treating cells *in vitro* with an effective dose of a substance that impairs cellular peptide processing for MHC presentation,

wherein the substance is characterized in that tumor cells treated with the substance are subject to specific lysis by CTL elicited by endogenous MHC class I dependent antigens of the TAP-deficient variant of said tumor cell which has been transfected with the stimulatory molecule B7-1; and

identifying cells which activate CD8+ T lymphocytes that selectively recognize cells showing endogenous epitopes associated with impaired cellular peptide processing for MHC presentation.

149. (New) A process according to claim 148, wherein the substance inhibits the function and/or expression of TAP.

150. (New) A process according to claim 149, wherein the substance is selected from the group consisting of ICP47 of HSV type 1, IE 12 of HSV type 2, a nucleotide sequence encoding a TAP inhibitor, a nucleotide sequence encoding that is complementary at least in part to the mRNA or DNA sequences encoding TAP, antisense oligonucleotides, and RNA-destroying ribozyme.

151. (New) A process according to claim 148, wherein the substance inhibits the function and/or expression of the proteasome.

152. (New) A process according to claim 151, wherein the substance is selected from the group consisting of a peptide aldehyde Z-Leu-Leu-H, Lactacystin, a nucleotide sequence encoding a proteasome inhibitor, a nucleotide sequence that is complementary to an mRNA or DNA sequence encoding proteasome, antisense oligonucleotides and RNA-destroying ribozyme.

153. (New) A process according to claim 148, wherein the cells are autologous and/or hematopoetic cells.

154. (New) A process according to claim 153, wherein the autologous and/or hematopoetic cells are dendritic cells or cells from cancer tissues.

155. (New) A process comprising

a) stimulating isolated immunological effector cells in vitro with cells identified according to the method of claims 148; and

b) identifying immunological effector cells that selectively recognize cells showing impaired cellular peptide processing for MHC presentation.

156. (New) The process of claim 155, wherein the immunological effector cells are CD8+ T lymphocytes.

157. (New) A composition comprising cells identified according to the method of claim 148.

158. (New) A process comprising

administering to a mammal immunological effector cells that selectively recognize cells showing impaired cellular peptide processing for MHC presentation.

159. (New) A composition comprising

a substance that impairs cellular peptide processing for MHC presentation,

and thereby induces immunological effector cells specific for endogenous epitopes associated with impaired cellular peptide processing for MHC presentation,

the substance being characterized in that tumor cells treated with the substance are subject to specific lysis by CTL elicited by endogenous MHC class I dependent antigens of the TAP-deficient variant of said tumor cell which has been transfected with the stimulatory molecule B7-1; and

a pharmaceutically acceptable adjuvant selected from cytokines, genes for cytokines, costimulatory molecules, gold beads and/or liposomes.

160. (New) A composition comprising

cells identified according to the method of claim 148, or antigens or epitopes expressed by such cells; and

a pharmaceutically acceptable additive.

161. (New) A composition comprising immunological effector cells identified according to the method of claim 155.

162. (New) A kit comprising

a substance that impairs cellular peptide processing for MHC presentation, and thereby inducing immunological effector cells specific for endogenous epitopes associated with impaired cellular peptide processing for MHC presentation,

the substance being characterized in that tumor cells treated with the substance are subject to specific lysis by CTL elicited by endogenous MHC class I dependent antigens of the TAP-deficient variant of said tumor cell which has been transfected with the stimulatory molecule B7-1; and

cytokines, DNA encoding cytokines, costimulatory molecules, gold beads and/or liposomes.